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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/650,074	08/28/2003	Michael James Paul Arthur	117-473	7212

23117 7590 11/21/2006

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EXAMINER
HIRIYANNA, KELAGINAMANE T

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 11/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/650,074	ARTHUR ET AL.	
	Examiner	Art Unit	
	Kelaginamane T. Hiriyanna	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 August 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,11,24-28 and 30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,11,24-28 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/22/06 &10/23/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 8/22/2006 in response to office action mailed on 03/22/2006 has been acknowledged.

Claims 3-8, 15-16, 23 and 29 are cancelled

Claims 1, 11, 24, 28 are amended

Claim 30 is newly added

Claims 1-2,11, 24-28 and 30 *are pending and are examined in this office action. Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is* ***571-273-8300.***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

Claim Rejections - 35 USC § 112

(I). Claims 1-2, 11, 24 and 28 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for the reasons of record set forth in the previous office action applied here for the following scope of the invention after amendments and cancellation of claims in response to office action mailed 03/22/06.

The scope of the instant claims encompass a method of treating a liver fibrosis in a subject comprising administering by administering by any mode to said subject an effective amount of sulfasalazine and any and/or all derivatives thereof that are capable of inducing hepatic cell apoptosis.

Response to Arguments (8/22/2006)

The Applicant amends and cancels claims as indicated earlier. The Applicant does not specifically address the cited breadth of the claims as above. The Applicant further argues that the present application describes claimed

inducers of HSC and their delivery to treat liver fibrosis and thus providing adequate written description.

This is found not persuasive because the instant specification only provides guidance and/or evidences regarding assessment of effect of sulfasalazine on hepatic stellate cells grown in vitro or in vivo experiments.

The specification however, does not present representative number of sulfasalazine derivatives used in liver fibrosis therapy or their administration methods to support the broad claims.

Given the relative paucity or absence of evidences in the art regarding claimed use of sulfasalizine or its derivatives in the treatment of a liver fibroses it is incumbent upon the applicant to provide enabled descriptions of the broadly claimed derivatives and their routes of administration and further in sufficient number of examples to support the full scope and breadth of the claims. To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail such that the Artisan can reasonably conclude that the inventor(s) had possession of the claimed invention. Such possession may be demonstrated by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and/or formulae that fully set forth the claimed invention. Possession may be shown by an actual reduction to practice, showing that the invention as claimed is "ready for patenting", or by describing distinguishing identifying characteristics sufficient to show that applicant was in possession of the claimed invention (January 5, 2001 Fed.Reg. Vo.66, No. 4, pp. 1099-11). The specification fails to disclose any sulfasalazine derivative whih is capable of treating liver fibrosis. According to these facts, one of skill in the art would conclude that applicant was not in possession of the claimed genus because a description of even a single member of the genus would not be representative of number of possible species of derivatives of sulfasalazine and is insufficient to support them.

(II). Claims 1-2, 11, 24-28 and 30 stand rejected are rejected under 35 U.S.C. 112 first paragraph (enablement) for the reasons of record set forth in the previous office action in response to office action mailed 03/22/06.

The scope of the instant claims encompass a method of treating a liver fibrosis in a subject administering of sulfasalazine and/or its derivatives thereof that are capable of inducing hepatic cell apoptosis by any mode of administration to said subject and in further limitation claims the use of liver implants to deliver using liposomes.

Response to Arguments (8/22/2006)

The Applicant amends and cancels claims as indicated earlier. The Applicant further argues that the present application describes claimed inventions adequately and the application provides experimental evidence showing sulfasalazine can be used to treat liver fibrosis in an accepted model of the condition.

However, this is found not fully persuasive because the invention as claimed is not fully enabled. One of skilled in the art would not be able to rely upon the state of the art to successfully predict a priori that any derivative of sulfasalazine induces selective apoptosis of hepatic stellate cells and further will not be able to predict that any said derivative is therapeutically usable. For example Liptay et al.,(1999, British Journal of Pharmacology 128:1361-1369) indicates that 5ASA and sulfapyridine neither inhibit NF-kB/Rel activation nor induce apoptosis in T-lymphocytes at doses up to 5.0 mM and hence not be able to subsequently clear the activated cells. Thus the relevant art reads away from using any derivatives of sulfasalazine to induce apoptosis. Further, applicant does not describe enabled examples specific delivery of sulfasalazine derivative using a liver implant and liposomes. Accordingly, in view of the lack of teachings in the art and lack of guidance provided by the specification with regard to representative number of enabled examples of sulfasalazine derivatives used for treating liver fibrosis via hepatic cell specific apoptosis and in view of lack of an enabled use of a method of treatment of a hepatic fibrosis by claimed specific delivery of sulfasalazine using a liver implant as of filing date of instant

application and for the specific reasons cited previously, it would have required undue experimentation for one of skill in the art to make and use the full scope of the claimed invention.

Applicants' attention is drawn to In re Shokal, 242 F.2d 771, 113 USPQ 283 (CCPA 1957). The test is whether the species completed by applicants prior to the reference date or the date of the activity provided an adequate basis for inferring that the invention has generic applicability. Examiner, having read the instant specification broadly in the light of the Art, finds that such is not the case and hence concludes that the instant application does not reasonably provide enablement for the full breadth and scope of the claims and would have required undue experimentation for a skilled artisan to make and use the full scope of the methods as claimed.

Claim Rejections - 35 USC § 103

(III). Claims 1-2, 11, 24-28 and 30 stand rejected under 35 USC 103 (a) as being unpatentable over Lang et al., (1999, Ital. J. Gastroenterol. Hepatol. 31:173-179) and further in view of Liptay et al.,(1999, British Journal of Pharmacology 128:1361-1369) for the reasons of record set forth in the previous of mailed on 03/22/2006.

Response to Arguments (8/22/2006)

The applicant argues that nothing in the two documents either alone or in combination with each other, would have led the skilled person to employ sulfasalazine to treat liver fibrosis as specified by claim 1 because the skilled person considered that artificially inducing apopotosis would have had detrimental effect, rather than therapeutic effect.

However this is found not persuasive because the prior art clearly teaches that the clearance of activated hepatic stellate cells, which were considered as the major source of extracellular matrix in hepatic fibrosis wherein apoptosis is the main mechanism behind terminating the activated HSCs during the resolution of hepatic fibrosis (see Lang et al., Absract, p.173, col.2, p.176, 2nd paragraph). Further it was very clear that inhibitors of NFkB pathway would pave the way for

treating hepatic fibrosis. At that juncture, Litpay reference provides clear evidence to show that sulfasalazine is one such inhibitor. Thus it would have been obvious for one of ordinary skill in the art to use the sulfasalazine to inhibit NKkB pathway in the activated HSCs making them progress into apoptosis and thereby resolve accumulation of fibrotic material in the liver due to activated HSCs. The combination cited of references and the art reviewed in their thus completely address all the limitations of the instant invention. One skilled in the art would have had a reasonable expectation of success of using sulfasalazine for promoting activated stellate cell apoptosis as sulfasalazine is available from commercial sources and further the art (For example see Lang et al review) at the time of instant invention had established several systems for both in vitro and in vivo testing of the drugs or compounds with a potential to enhance apoptosis by inhibiting NF-kB pathway (For example TNF-alpha induces apoptosis in activated HSCs in culture by inhibiting NF-kB, p.177, conclusion and references). Litpay meanwhile establishes sulfasalazine induces apoptosis of T-lymphocytes by inhibiting NF-kB. Thus the instant invention was clearly made obvious to one of skill in the art by the combination of cited prior art.

Conclusion:

No claim allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Kelaginamane Hiriyanna* whose telephone number is **(571) 272-3307**. The examiner can normally be reached Monday through Friday from 9 AM-5PM. Any inquiry concerning this communication or earlier

communications regarding the formalities should be directed to Patent Analyst *William N. Phillips* whose telephone number is ***571 272-0548.*** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Dave Nguyen*, may be reached at **(571) 272-0731.** The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). When calling please have your application serial number or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. For all other customer support, please call the USPTO call center (UCC) at (800) 786-9199.

Kelaginamane T. Hiriyanna

Patent Examiner

Art Unit 1633

SUMESH KAUSHAL, PH.D.
PRIMARY EXAMINER